

I. **AMENDMENTS TO THE CLAIMS**

Claim 1. (Currently Amended) A compound of formula (I) or a salt thereof ~~which are able to release COX-2 inhibitors and NO (nitrogen oxide) under conditions and according to the parameters set up in test 1 mentioned in the description~~



(I)

wherein:

M-T is the residue of M-TH or M-TOH,

wherein M-TH and M-TOH are [[a]] COX-2 selective inhibitor inhibitors, in which wherein T = -SO₂NH-, -SO₂NR-, -CO-, -O-, -S-, -NH-, -N(SO₂R)-, R being an alkyl with 1-10 carbon atoms, and

wherein the COX-1 inhibiting activity/COX-2 inhibiting activity ratio (IC₅₀) of the COX-2 selective inhibitor, M-TH or M-TOH, has to meet test 2 mentioned in the description is greater than or equal to 5,

$Y_A = -(B)_{b0}-(C)_{c0}-(B)_{b0}-(T_C-Y)_{c0}$ wherein:

b0 [[e]] and c0 are the integers 1 or 0, with the proviso that b0 and c0 cannot be simultaneously 0,

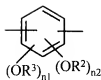
B = -T_B-X₂-T_{BI}-, in which:

T_B = CO or X, wherein X = O, S, NH, NR, and R is as defined above, T_B is CO when T is -SO₂NH-, -SO₂NR-, -O-, -S-, -NH-, or -N(SO₂R)-[[.]]; and T_B is X when T is -CO-;

T_{BI} = CO or X, in which X is as defined above;

X₂ is a divalent radical and is selected from the following compounds:

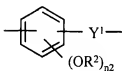
a)



wherein:

$n1$ and $n2$ are integers 0 or 1; R^2 and R^3 are independently selected from H or CH_3 ;

b)

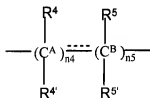


wherein:

$n2$ and R^2 are as above defined;

Y^1 is $-CH_2-CH_2-$ or $-CH=CH-(CH_2)_{n2}-$ wherein $n2'$ is an integer 0 or 1;

c)



wherein:

$n4$ is an integer from 1 to 20 and $n5$ is an integer from 0 to 20[[.]]; R^4 , $R^{4'}$, R^5 and $R^{5'}$ are independently selected from the group consisting of H, CH_3 , OH, NH_2 , $NHCOCH_3$, and $COOH$; when the bond between the C^A and C^B carbons is a double bond, then R^4 and R^5 or $[[R^{4'}]]$ $R^{4'}$ and $[[R^{5'}]]$ $R^{5'}$ are absent;

G is the bivalent radical $-T_C-Y-$, wherein:

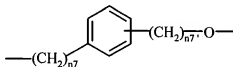
$T_C = CO, X$ wherein X is as defined above, or $-(CH_2)_{n6}OC(O)-$ wherein $n6$ is an integer from 1 to 20;

Y is a bivalent radical having the following meanings:

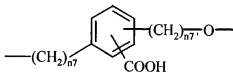
d) $-R^1O-$, in which R^1 is:

- straight or branched C_1 - C_{20} -alkylene optionally containing one or more heteroatoms selected from oxygen, nitrogen, sulphur, or one or more groups $-O(CO)-$, $-NH(CO)-$, $-S(CO)-$, optionally substituted with one or more of the following groups $-OH$, $-SH$, $-NH_2$, $-NHCOR^6$, in which R^6 is straight or branched C_1 - C_{10} -alkyl;
- cycloalkylene containing from 5 to 7 carbon atoms into cycloalkylene ring, wherein one or more carbon atoms can be replaced by heteroatoms selected from nitrogen, oxygen or sulphur, and the ring can be substituted with side chains R^6 , R^6 being as defined above;

e)

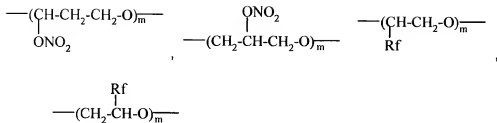


f)



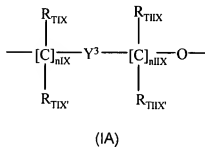
wherein $n7$ is an integer from 0 to 20, and $n7'$ is an integer from 1 to 20;

g)



wherein m is an integer from 1 to 6, Rf is a hydrogen atom or CH₃;

h)



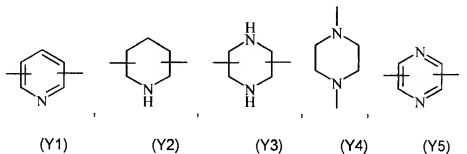
wherein:

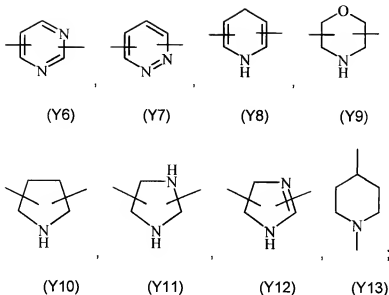
nIX is an integer from 0 to 10;

nIIX is an integer from 1 to 10;

R_{TIX}, R_{TIX'}, R_{TIIIX}, R_{TIIIX'}, are the same or different, and are H or straight or branched C₁-C₄-alkyl;

Y³ is an heterocyclic saturated, unsaturated or aromatic 5 or 6 members ring, containing one or more heteroatoms selected from nitrogen, oxygen, sulphur, and selected from





with the proviso that:

when $b_0 = 0$, $c_0 = 1$ and $T = -SO_2NH-$, $-SO_2NR-$, $-O-$, $-S-$, $-NH-$, $-N(SO_2R)-$ wherein R is as defined above, then $T_C = (CO)$ or $-(CH_2)_{n_6}O(CO)-$;

when $b_0 = 0$, $c_0 = 1$ and $T = CO$ then $T_C = X$ wherein X is as defined above;

when $b_0 = 1$ and $T = -SO_2NH-$, $-SO_2NR-$, $-O-$, $-S-$, $-NH-$, $-N(SO_2R)-$ wherein R is as defined above, then $T_B = CO$;

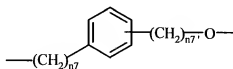
when $b_0 = 1$ and $T = CO$ then $T_B = X$ wherein X is as defined above;

when $b_0 = 1$, $c_0 = 1$ and $T_{B1} = CO$ then $T_C = X$ wherein X is as above defined;

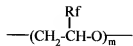
when $b_0 = 1$, $c_0 = 1$ and $T_{B1} = X$, wherein X is as above defined, then $T_C = (CO)$;

when $b_0 = 1$, $c_0 = 0$ the T_{B1} has only the meaning of $-O-[[:]]$.

Claim 2. (Original) A compound of formula (I) according to claim 1 wherein $b_0 = 0$, $c_0 = 1$, T and T_C are as defined in claim 1, Y is a straight C_1 - C_6 alkylene or



wherein n_7 is 0 or 1, and n_7' is 1 or 2, or



wherein m is 2, Rf is hydrogen.

Claim 3. (Original) A compound of formula (I) according to claim 2 wherein $b_0 = 0$, $c_0 = 1$, $\text{T} = \text{---N}(\text{SO}_2\text{R})\text{---}$, $\text{T}_c = \text{CO}$ or $\text{---}(\text{CH}_2)_{n_6}\text{O}(\text{CO})\text{---}$ wherein $n_6 = 1$ and $\text{R} = \text{CH}_3$.

Claim 4. (Currently Amended) A compound of formula (I) according to claim 2 wherein $b_0 = 0$, $c_0 = 1$, $\text{T} = \text{---SO}_2\text{NH---}$ and $\text{T}_c = \text{CO}$ or $\text{---}(\text{CH}_2)_{n_6}\text{O}(\text{CO})\text{---}$ wherein $[[n_6]]$ n_6 = 1.

Claim 5. (Currently Amended) A compound of formula (I) or a salt thereof according to claims 1 to 4 wherein M-T is $[[e]]$ a residue of a COX-2 selective inhibitor of formula M-TH or M-TOH selected from the group consisting of 4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide, 4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]-methanesulfonamide, N-(4-nitro-2-phenoxyphenyl)methanesulfonanilide, N-(4-nitro-2-cyclohexyloxyphenyl)methane sulfonanilide, 2-[(2-chloro-6-fluorophenyl)amino]-5-methylbenzeneacetic acid, and 2-[(2-chloro-6-fluorophenyl)-amino]-4-methylbenzeneacetic acid.

Claim 6. (Original) A compound according to claim 3, that is N-[6-(2,4-difluorophenylthio)-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[(4-nitrooxy)butyroxymethyl]methanesulfonamide.

Claim 7. (Original) A compound according to claim 3, that is N-[6-(2,4-difluorophenylthio)-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[3-(nitrooxymethyl)benzoyloxymethyl]methanesulfonamide.

Claim 8. (Original) A compound according to claim 3, that is (Z)-2-(4-methylsulphonylphenyl)-3-phenyl-2-buten-1,4-diol-1-[(4-nitrooxymethyl)-benzoate]].

Claim 9. (Original) A compound according to claim 4, that is N-[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenylsulfonyl]-4-nitrooxybutanamide.

Claim 10. (Original) A compound according to claim 3, that is N-(3-nitrooxymethyl)benzoyloxymethyl-N-(2-phenoxy-4-nitrophenyl)methane-sulfonamide.

Claim 11. (Currently Amended) A compound of formula (I) or a salt thereof according to ~~claims 1-10 as~~ claim 1, wherein said compound is a therapeutic agent.

Claim 12. (Currently Amended) A method of ~~Use of a compound of formula (I) or a salt thereof according to claims 1-10, for preparing a drug that can be employed in the treatment or prophylaxis of inflammatory disorders, pain and fever, comprising~~

administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 13. (Currently Amended) ~~[[Use]]~~ A method according to claim 12, ~~characterized in that wherein~~ the inflammatory disorders are selected from the group consisting of, ~~but not limited to~~, arthritis, ~~reumatoid~~ rheumatoid arthritis, osteoarthritis, ~~diemenhorrea~~ dysmenhorrea, allergic rhinitis, sinusitis, chronic obstructive pulmonary diseases, dermatitis, psoriasis, cystic fibrosis, ~~multiple~~ multiple sclerosis, vasculitis and organ transplant rejection.

Claim 14. (Currently Amended) A method of ~~Use of a compound of general formula (I) or a salt thereof according to claims 1-10, for preparing a drug that can be employed in the treatment or prophylaxis of cardiovascular diseases, comprising~~ administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 15. (Currently Amended) ~~[[Use]]~~ A method according to claim 14, ~~characterized in that wherein~~ the cardiovascular diseases are selected from the group consisting of, ~~but not limited to~~, atherosclerosis, restenosis, coronary artery disease, angina, diabetes mellitus, diabetic nephropathy, diabetic retinopathy, stroke and myocardial infarct.

Claim 16. (Currently Amended) A method of ~~Use of a compound of general formula (I) or a salt thereof according to claim 1-10, for preparing a drug that can be employed in the treatment or prophylaxis of gastrointestinal disorders, comprising~~

administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 17. (Currently Amended) [[Use]] A method according to claim 16, ~~characterized in that wherein~~ the gastrointestinal disorders are selected from the group consisting of, ~~but not limited to,~~ inflammatory intestinal disorders, Crohn's disease, gastritis, ulcerative colitis, peptic ulcer, haemorrhagic ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison's syndrome, bacterial infections, hypersecretory states associated with systemic mastocytosis or basophilic leukaemia and hyperhystaminemia.

Claim 18. (Currently Amended) A method of Use of a compound of general formula (I) or a salt thereof according to claim 1-10, for preparing a drug that can be employed in the treatment or prophylaxis of tumors and Alzheimer's disease, comprising administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 19. (Currently Amended) A method of Use of a compound of general formula (I) or a salt thereof according to claim 1-10, for preparing a drug that can be employed for treating or preventing disorders resulting from elevated levels of COX-2, comprising administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 20. (Currently Amended) A method of [[Use]] according to claim 19, ~~characterized in that wherein~~ the disorders resulting from elevated levels of COX-2

are selected from the group consisting of ~~1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000~~, but not limited to, angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, tendinitis, bursitis, neoplasia, ophthalmic diseases, pulmonary inflammations, central nervous system disorders, allergic rhinitis, atherosclerosis, endothelial disorders, organs and tissues preservation, and inhibition and/or or prevention of platelets platelet aggregation.

Claim 21. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of general formula (I) or a salt thereof according to claim [[1-10]]1.

Claim 22. (Original) A composition according to claim 21 in a suitable form for the oral, parenteral, rectal, topic and transdermic administration, by inhalation spray or aerosol or iontophoresis devices.

Claim 23. (Currently Amended) ~~Liquid~~ A liquid or solid pharmaceutical composition for oral, parenteral, rectal, topic and transdermic administration or inhalation in the form of tablets, capsules and pills ~~eventually~~ on optionally with enteric coating, powders, granules, gels, emulsions, solutions, suspensions, syrups, elixir, injectable forms, suppositories, in transdermal patches or liposomes, containing a compound of formula (I) according to claim [[1-10]] 1 or a salt thereof and a pharmaceutically acceptable carrier.